



IN THE UNITED STATES DISTRICT COURT  
FOR THE SOUTHERN DISTRICT OF OHIO  
WESTERN DIVISION AT CINCINNATI

C-1-00 12735

DURAMED PHARMACEUTICALS, INC.,

CIVIL ACTION NO. \_\_\_\_\_

7155 East Kemper Rd.  
Cincinnati, Ohio 45249,

JURY TRIAL DEMANDED

Plaintiff,

J. BECKWITH

vs.

FILED

WYETH-AYERST LABORATORIES,  
INC.,

SEP 5 2000

150 N. Radnor Chester Road  
St. Davids, PA 19087,

KENNETH J. MURPHY, Clerk  
CINCINNATI, OHIO

Defendant.

**COMPLAINT**

**I.**  
**PARTIES**

1. Plaintiff Duramed Pharmaceuticals, Inc. ("Duramed") is a Delaware corporation with its principal place of business in Cincinnati, Ohio. Duramed is a pharmaceutical company that develops, manufactures, and markets prescription and over-the-counter drug products. Among its current products is a conjugated estrogens drug product for women sold under the trademark of Cenestin®.

2. Defendant Wyeth-Ayerst Laboratories, Inc. ("Wyeth") is a Delaware corporation that regularly transacts business in this judicial district. Wyeth is also a pharmaceutical company that, among other drug products, since 1942, has been manufacturing and marketing a conjugated estrogens drug product for women sold under the trademark of Premarin®.

**II.**  
**JURISDICTION AND VENUE**

3. This action is brought under the antitrust laws contained in 15 U.S.C. § § 1, 2, and 14 *et. seq.* Under 28 U.S.C.A. § 1331, this Court has jurisdiction to adjudicate this dispute.

4. Venue in this jurisdiction is proper under Clayton Act §§ 4 and 12, 15 U.S.C. §§ 15 and 22; and 28 U.S.C. 1391. Wyeth regularly transacts business and is subject to personal jurisdiction in this jurisdiction through the marketing, sale and distribution of Premarin and other pharmaceutical drugs. A substantial portion of the events giving rise to Duramed's claim and damages occurred in this jurisdiction.

**III.**  
**NATURE OF THE CASE**

5. This is an antitrust case. Since 1942, Wyeth has been manufacturing and marketing a prescription drug for women called Premarin, derived from pregnant mares' urine, designed to relieve moderate-to-severe vasomotor symptoms (hot flashes and night sweats) associated with menopause.

6. Although its patent protection for Premarin expired long ago, as a result of its anti-competitive and exclusionary conduct, as discussed throughout this complaint, Wyeth has enjoyed and currently enjoys a monopoly of the conjugated estrogens market (maintaining a current market share of approximately 99%), and reaps well over \$800 million in annual U.S. sales of Premarin—the most widely prescribed drug in the United States. Wyeth's revenues from the sales of Premarin are in part attributable to its price increases of the drug. Between January 1999 and January 2000, Premarin experienced one of the largest price increases of any single source

prescription drug—12.1 %, a rate which is 5 ½ times the rate of inflation. Effective March 29, 2000, Wyeth raised Premarin's price by 6.2%.

7. Wyeth prevented Duramed from offering on the market a generic conjugated estrogens drug product that would have been a plant-derived, less expensive alternative to Wyeth's drug Premarin, similarly indicated for moderate-to-severe vasomotor symptoms associated with menopause. Wyeth has maintained its monopoly over the conjugated estrogens market by petitioning the U.S. Food and Drug Administration ("FDA") to deny approval of Duramed's Abbreviated New Drug Application (ANDA) for its generic conjugated estrogens drug, by supplying the FDA misinformation about its own and Duramed's product, and by engaging in a host of other anti-competitive conduct detailed in this complaint. In the late 1980s and early 1990s, Wyeth manipulated and convinced the FDA to remove from the market all generic conjugated estrogens drug products, including Duramed's. From 1994 to 1997, Wyeth orchestrated a misleading political and public relations campaign which, ultimately, persuaded the FDA to deny Duramed's application for approval of a generic conjugated estrogens.

8. Because Wyeth succeeded in its anti-competitive campaign in keeping Duramed's generic conjugated estrogens drug product off the market, Duramed had no choice but to apply to the FDA for approval of a New Drug Application ("NDA") for a brand name conjugated estrogens drug product called Cenestin, which was identical in composition to Duramed's proposed generic conjugated estrogens drug. Again, in efforts to preclude all competition in the conjugated estrogens market, Wyeth vehemently opposed Duramed's application to the FDA. This time, however, Wyeth's efforts failed; in March 1999, the FDA approved Duramed's application for Cenestin for use in the treatment of the symptoms of menopause (approximately 3 years and tens of millions of

dollars in expenditures after Duramed's generic conjugated estrogens drug product should have been approved).

9. Wyeth, however, would not give up easily its dominant position in the market, and devised a scheme to preclude Duramed from reaping the benefits of its enduring and costly efforts to get Cenestin to market. Since March 1999, Wyeth has hampered Cenestin's success in the market through various anti-competitive and exclusionary acts designed to perpetuate its monopoly over the conjugated estrogens market, including issuing information about Cenestin designed to discourage consumers from purchasing it and using exclusive and "disguised" exclusive contracts with health plans and pharmacy benefits managers ("PBMs"), which either preclude or discourage, by means of financial incentives, these entities from placing Cenestin on their drug formularies. The preclusion from formularies has resulted in significantly lower than expected sales of Cenestin.

10. Throughout its opposition to all competition in the conjugated estrogens market and its perpetuation of a monopoly, Wyeth has continued to increase the price of Premarin and reap the benefits of a monopoly. Wyeth's monopolization of the market through anti-competitive and exclusionary conduct has not only proximately caused Duramed millions of dollars in damages, but has also deprived women suffering from menopausal symptoms of a plant-derived, lower cost conjugated estrogens alternative to Premarin.

**IV.**  
**BACKGROUND FACTS**

A. About Conjugated Estrogens – Premarin and Cenestin

11. Menopause is a normal part of a woman's aging process. The average age of a menopausal woman is 51, and it is estimated that, at this time, there are over 700 million women throughout the world entering or in the menopausal phase of their lives.

12. Technically, menopause is the female ovaries' loss of ability to produce estrogen and progesterone, two hormones that govern the menstrual cycle. Loss of estrogen can cause vasomotor symptoms, such as hot flashes and night sweats, as well as other physiological changes and discomforts. Estrogen replacement can alleviate these symptoms and is important in protecting a woman's body from significant health risks.

13. Since 1942, Wyeth has been manufacturing and marketing Premarin, a conjugated estrogens prescription drug product, initially for relief of uncomfortable vasomotor symptoms. In 1986, FDA approved an additional indication, the prevention of osteoporosis. The drug product is derived from pregnant mares' urine, hence the name Premarin. The manufacturing of Premarin involves the process of keeping over tens of thousands of pregnant horses in a small, confined place during much of their pregnancy so that estrogens can be collected from the mares' urine and processed into a bulk active drug substance. The bulk active drug substance is combined with inactive ingredients and formed into a tablet. The Premarin tablet is then coated in shellac, which functions as a release agent and masks the drug's urine flavor and odor.

14. In the Physicians' Desk Reference, Premarin is classified as "conjugated estrogens tablets USP." "Conjugated estrogens" means a mixture (with defined parameters of percentages)

of sodium estrone sulfate and sodium equilin sulfate, derived wholly or in part from equine urine or synthetically from estrone and equilin, that is released into the system in a modified fashion. The USP designation in the name signifies that Premarin complies with the definition of conjugated estrogens contained in the United States Pharmacopeia ("USP"), which publishes the United States' official compendium of pharmaceuticals, a listing that is essential to a drug's acceptance by the medical community.

15. In 1942, the FDA approved Premarin under the Federal Food, Drug, and Cosmetics Act ("FDCA"), which did not require a comprehensive analysis of drug products seeking FDA's approval. To obtain the FDA's approval to market the drug, Wyeth had to show only the drug's safety—that the drug was not toxic. At that time, the FDA did not require new drug applicants to prove the drug's efficacy—that it actually worked for the symptoms for which it was indicated. Not until the U.S. Congress passed the 1962 amendments to the FDCA were drug manufacturers required to show both the drug's safety and efficacy. To the present day, Wyeth has never identified all of Premarin's active ingredients, as well as any required "concomitant" components or impurities, as would a drug applicant today.

16. In recent years, Premarin has become the most widely prescribed drug in the United States. Over 8 million women each year take Premarin to treat menopausal symptoms. In the United States alone, Wyeth sells annually approximately \$800 million of Premarin.

17. In or about March 1998, Duramed, a Cincinnati-based pharmaceutical company, submitted its NDA for a brand name drug product called Cenestin. Cenestin is a plant-derived conjugated estrogens product that, like Premarin, is indicated for the treatment of moderate-to-severe vasomotor symptoms associated with menopause in women. Cenestin is derived from soy and yam

plants and is synthesized into a drug product using a modern manufacturing process that insures a quality product with a uniform release of the drug into a woman's system. Not only does Cenestin offer a plant-derived choice of medication, Cenestin's average wholesale price is approximately 14-26 % less per tablet than Premarin's. In March 1999, Duramed received FDA's approval to market Cenestin. Until March 1999, Premarin was the only available brand named conjugated estrogens drug product for menopausal symptoms on the U.S. market. Today, there are only two brands of conjugated estrogens drugs on the market — Premarin and Cenestin. There is no generic conjugated estrogens drug product on the market. Wyeth currently enjoys approximately a 99% share of the conjugated estrogens market.

18. In the face of Wyeth's efforts to block market access to any drug that would compete with Premarin, Duramed succeeded in bringing a brand name drug—Cenestin—to market. Cenestin's approval, however, came at a heavy price. Wyeth's anti-competitive conduct in keeping Duramed's generic conjugated estrogens drug product off the market cost Duramed years of profits and the investment of millions of dollars over and above the cost of bringing a generic drug to market. Not satisfied with having crushed all generic competition, in 1998, Wyeth even vehemently opposed, albeit unsuccessfully, the FDA's approval of Duramed's brand name conjugated estrogens drug product—Cenestin. In spite of Duramed's accomplishment of getting Cenestin to market as an alternative conjugated estrogens for women, Wyeth continues to engage in anti-competitive and exclusionary conduct that is designed to prevent the success of Cenestin and to preserve Wyeth's illegal monopoly over the conjugated estrogens market.

B. In the 1980s and 1990s, Wyeth Succeeds in Eliminating Competition from All Generic Conjugated Estrogens on the Market

19. Since 1970, the USP has defined conjugated estrogens as drugs containing primarily the active components sodium estrone sulfate and sodium equilin sulfate. In or about 1972, the FDA reviewed a number of estrogen products, including Premarin, and published a Federal Register Notice that these drugs have been shown to be effective in the treatment of menopausal symptoms. In the same notice, the FDA provided guidelines for the submission and approval of ANDAs for generic conjugated estrogens drug products, and stated that the applicants were not required to show their drugs' bioequivalence—the therapeutic equivalence of a generic with the name brand drug that it was emulating.

20. Generally, generic drugs cannot be marketed until after the patent on the branded drugs being copied has expired. Because Premarin's patent expired long ago and given that the FDA issued new guidelines on generics, in the early to mid-1980s, pharmaceutical companies such as Zenith Labs, Private Formulations, Inc., Cord Laboratories, West Ward Pharmaceuticals and others, including Duramed, developed and sought FDA's approval for generic conjugated estrogens. By 1985 - 1986, the FDA approved several ANDAs for various generic conjugated estrogens, including a generic conjugated estrogens drug available in four different dosage strengths that Duramed manufactured.

21. Also in or about 1986, Wyeth began its aggressive campaign to convince the FDA that all the generic conjugated estrogens on the market were not the "generic equivalent" of Premarin because Premarin was the only conjugated estrogens with a modified release versus an immediate release of estrogen into a woman's system. Through voluminous correspondence, Wyeth

attempted to convince the FDA that immediate releases of estrogens could produce higher blood concentrations of estrogens that could cause harmful health effects, such as endometrial cancer.

22. Wyeth's communications with the FDA were highly deceptive. First, Premarin's modified release had not been proved by any reliable scientific data. In support of its assertions, Wyeth did not even submit studies that would measure the levels of estrogen release. Second, Wyeth's manufacturing process for Premarin undermines its claim of a modified release of its product. Because Premarin is coated with shellac, a substance which is prone to aging and cracking, Premarin cannot guarantee that consistent estrogen levels are released into the body in a modified manner. Third, while focusing the FDA's attention on the danger of an immediate release characteristic of conjugated estrogens, its Premarin product manufactured and marketed in Canada contained a different, and faster, estrogen release than its U.S. product.

23. Based on Wyeth's deceptive information, the FDA decided to reclassify all the synthetic conjugated estrogens products to a "BP" classification, namely, to describe a drug that could have potential bioequivalence problems, and required the generic conjugated estrogens manufacturers to perform plasma studies on their drugs to demonstrate their bioequivalence to Premarin.

24. Following completion of these studies, in or about February 1990, the FDA determined that this varied release could render the conjugated estrogens ineffective in treating osteoporosis, and could pose a significant health risk to patients. Before the FDA held its hearing on whether to withdraw approval of the ANDAs of all conjugated estrogens on the market, in February 1991, Duramed voluntarily surrendered its ANDA approvals. All other generic conjugated estrogens manufacturers similarly surrendered their approvals.

25. In this way, Wyeth's efforts resulted in the removal of all generic conjugated estrogens from the market. Wyeth once again restored its complete monopoly on the conjugated estrogens market. In keeping with its monopoly power, Wyeth continued to raise the price of Premarin.

C. Wyeth Successfully Opposes Competition from Duramed's Improved Modified Release Generic Conjugated Estrogens

26. After surrendering its ANDA for a generic conjugated estrogens drug, Duramed turned its attention to developing a generic product that would meet the FDA's new standards on modified release. Starting in October 1991, Duramed spent approximately two (2) years developing its improved conjugated estrogens drug product.

27. During this time period, the Code of Federal Regulations provided that an ANDA must include information that shows that the drug is the bioequivalent to the brand name product, or the reference listed drug, on which the applicant relies. Among the criteria required to show bioequivalence is that the proposed drug contains the same active ingredients as the reference listed drug. In the case of Premarin, as discussed, since 1970, the USP considered conjugated estrogens to have two active ingredients: sodium estrone sulfate and sodium equilin sulfate. In September 1991, however, based on Wyeth's persistence, the FDA got the USP to change its definition of conjugated estrogens to: sodium estrone sulfate, sodium equilin sulfate, and three (3) non-active "concomitant" components that must be present in a conjugated estrogens drug, but that would not be considered active ingredients. Significantly, at this time, the FDA considered the delta<sup>8,9</sup>-DHES present in Premarin neither an active ingredient nor a required concomitant component. At that time,

delta<sup>8,9</sup>-DHES was considered an impurity that was not required to be present in a generic version of Premarin.

28. Having removed from the market all generic conjugated estrogens in order to continue its long-lasting monopoly on the market, Wyeth began an aggressive effort to get the FDA to recognize delta<sup>8,9</sup>-DHES as a required concomitant component of conjugated estrogens. The FDA continued to reject Wyeth's position because it saw no justification for the reclassification. As late as May 1994, the FDA confirmed its position by writing to Wyeth: "Delta<sup>8,9</sup>-dehydroestrone is currently classified as an ordinary impurity."

29. After extensive research, tremendous expenditures, and state-of-the-art testing to demonstrate its bioequivalence to Premarin, in or about September 1994, Duramed filed with the FDA an ANDA to manufacture and market a generic conjugated estrogens drug. To be approved as a generic drug, the FDA required applicants to follow its prescribed guidelines and to match the active ingredients in the branded drug product, thereby demonstrating that the generic version possesses the same strength, dosage and potency as the brand name product. Duramed followed with precision the FDA's guidelines for manufacturing a generic conjugated estrogens product and matched all the active ingredients and the three (3) concomitant components that the FDA and the USP required for a conjugated estrogens drug product.

30. Duramed's process for manufacturing a synthetic, generic conjugated estrogens product was a different manufacturing process than the one that had been used in the past. Duramed obtained a patent on the process. Duramed's ANDA application was comprehensive, containing over 80 volumes of supporting scientific data for the application. Duramed's ANDA also overcame problems concerning the drug's stability and dissolution characteristics. In other words, through the

diligence and expertise of its scientists, Duramed insured that its generic conjugated estrogens drug would retain its strength over the shelf life of the product, and that the active ingredients in the drug would be absorbed into the system at the same rate as the active ingredients of the reference listed drug Premarin.

31. In 1995, the FDA led Duramed to believe that its review of the ANDA was complete based on Duramed's compliance with all of FDA's requirements, and that the approval of its generic drug was imminent.

32. Within a few months of Duramed's ANDA submission to the FDA, Wyeth stepped up yet again its aggressive efforts to prevent any competitor from entering the conjugated estrogens market. This time, to protect its monopoly on the conjugated estrogens market and its 1994 Premarin sales of approximately \$853 million, Wyeth waged a battle against FDA's approval of Duramed's generic conjugated estrogens.

33. In or about November 1994, Wyeth filed two Citizen Petitions with the FDA—"Citizen Petition to Establish the Proper Composition of Conjugated Estrogens and Conjugated Estrogens Tablets," and "Petition for Stay of Action—Approval of ANDAs for Conjugated Estrogens Products Not Containing Sodium Delta<sup>8,9</sup>-Dehydroestrone." In its petitions, Wyeth requested that the FDA take the following action: (a) recognize an impurity in Premarin, delta<sup>8,9</sup>-DHES, as a required concomitant component of conjugated estrogens; (b) amend the USP for conjugated estrogens to include delta<sup>8,9</sup>-DHES as a required concomitant component of conjugated estrogens; and (c) not accept Duramed's ANDA because it did not contain delta<sup>8,9</sup>-DHES. In short, Wyeth sought to preclude approval of any generic version of Premarin that did not contain delta<sup>8,9</sup>-DHES.

At all relevant times, delta<sup>8,9</sup>-DHES was not commercially available and no generic version of Premarin could contain this impurity.

34. While Wyeth characterized the presence of delta<sup>8,9</sup>-DHES in Premarin as a safety issue, Wyeth presented no scientific or other data to support such a safety allegation. Nor could the presence of this compound be legitimately considered an efficacy issue. As discussed, the FDA approved Premarin for vasomotor symptoms in 1942, and for osteoporosis in 1986. The FDA had previously approved other non-conjugated estrogens, such as Ogen<sup>®</sup> and Estrace<sup>®</sup>, for the same indications. Neither Ogen nor Estrace contained (nor contain today) delta<sup>8,9</sup>-DHES.

35. During the time that the FDA was considering Duramed's pending ANDA, Wyeth began corresponding with the FDA and providing it misleading data of its internal, scientific studies in the hopes of confusing the agency as to the true active ingredients contained in Premarin. During the pendency of the FDA's review of Duramed's ANDA and Wyeth's Citizen Petitions, Wyeth fabricated, falsified, and withheld from the FDA certain data which did not support the conclusions it was advocating in its petitions. Based on the FDA's internal review of Wyeth's scientific practices, an FDA independent investigator ultimately concluded that none of Wyeth's studies should be included in the FDA's review of Wyeth's petitions.

36. Further to its deceptive scheme to convince the FDA of the importance of delta<sup>8,9</sup>-DHES, Wyeth enlisted independent investigators—scientists and physicians in the community—to conduct tests on Premarin. Wyeth mislead these investigators into believing they were conducting studies on Premarin tablets, when instead, they were performing studies on either injectable forms of estrogen, a capsule form of estrogen in a higher dosage strength than Premarin, or some other forms of estrogen medication that were different from the Premarin tablets.

37. Wyeth's petitions to and correspondence with the FDA were just one part of the massive and deceptive public relations, legal and political efforts to preserve its lucrative monopoly. In addition to Wyeth's Citizen Petitions to the FDA, Wyeth persuaded members of Congress and various women's, consumer, and professional groups to write to the FDA in opposition to Duramed's generic conjugated estrogens based on Wyeth's misinformation to these groups that the lack of delta<sup>8,9</sup>-DHES was somehow critical to the integrity of the drug.

38. Wyeth also circulated an anonymous "White Paper," which discussed that the absence of delta<sup>8,9</sup>-DHES may create significant health risks and fail to prevent osteoporosis. It falsely implied that delta<sup>8,9</sup>-DHES was an active ingredient in conjugated estrogens, and that the FDA was prepared to approve a generic drug without delta<sup>8,9</sup>-DHES solely because it was not commercially available. The paper also played on the fear of cancer, a risk which is associated with all products containing estrogen, including Premarin. Wyeth's paper concluded:

FDA's approving a generic version of Premarin which is not the same as Premarin would place unacceptable risk of uncertainty on an ever-increasing patient population of post-menopausal women facing a major health problem.

39. The success of Wyeth's efforts was evident from the support of members of Congress and women's groups that flooded the FDA with letters, all of which were similar in style, urging the agency to disapprove a generic version of Premarin. For example, on March 16, 1995, the Society for Advancement of Women's Health Research wrote:

It is my understanding that the generic product under [the FDA's] consideration is missing an active ingredient, delta<sup>8,9</sup>-DHES, that is present in the innovator drug, Premarin.

In certain instances, Wyeth would request that consumer groups to whom it provided substantial funding, write letters to the FDA, declaring that delta<sup>8,9</sup>-DHES was actually present in Premarin. In this way, Wyeth used its financial clout and influence over the FDA.

40. On February 27, 1995, Congresswomen Nita Lowey and Connie Morrell wrote:

. . . . if it is true that the FDA is about to approve a generic substitute for Premarin that does not contain the same active ingredient as Premarin, it would concern us greatly.

Also, in February 1995, Senator Barbara Mikulski wrote the FDA:

It is my understanding that the generic version does not possess the "same" active ingredients as the innovator, Premarin.

41. Also demonstrating its financial might, Wyeth threatened to withdraw funding of Yale University and other institutions which permitted their scientists to conduct studies for Cenestin and present their findings before the FDA, in this way assisting with its review of Duramed's ANDA. With the prospect of withdrawn funding, certain scientists who had committed to act as experts for Duramed, withdrew, thereby thwarting Duramed's efforts to obtain opinions and studies in support of its ANDA.

42. Finally, between January and March 1997, to insure the rejection of Duramed's ANDA for a generic conjugated estrogens, Wyeth flooded the FDA with letters that purported to identify the over twenty impurities contained in Premarin. FDA Commissioner Dr. Janet Woodcock did not share with Duramed this correspondence until after the rejection of its ANDA, thereby preventing Duramed from presenting any countervailing evidence to Wyeth's allegations. Wyeth attempted to provide the FDA with a scientific rationale that at least one of these impurities was an active ingredient in Premarin. Despite the fact that Duramed's ANDA for a generic conjugated

estrogens had met the USP's definition of conjugated estrogens, which contained no requirement of delta<sup>8,9</sup>-DHES and, at all times during the review process, received favorable feedback from the FDA, on May 5, 1997, the FDA rejected Duramed's ANDA.

43. In a memorandum to Douglas Sporn, Director of the Office of Generic Drugs, FDA's Director of the Center for Drug Evaluation and Research, Dr. Woodcock stated that Wyeth had not adequately characterized the active ingredients in Premarin and, therefore, the FDA could not recommend for approval a generic version of Premarin, despite its own guidelines which Duramed specifically followed. The FDA admitted that its decision was based on some new information supplied to it by Wyeth that threw into doubt the active ingredients of Premarin and the role of animal waste ingredients contained in Premarin. Dr. Woodcock described the FDA's decision in rejecting Duramed's ANDA as "very unusual," and a "complicated decision based on law and science." Dr. Woodcock also admitted that the agency's decision "ended up reversing a long-standing position of the agency," and reflected an "internally disputed policy change."

44. This decision was particularly shocking to Duramed, which was receiving favorable feedback from the FDA as late as two days prior to the FDA's rejection of its application. On May 3, 1997, the Office of Pharmaceutical Science's chief spokesperson on conjugated estrogens, Dr. Roger Williams, recommended in a report to Dr. Woodcock, that the FDA approve Duramed's generic conjugated estrogens drug and that the USP's definition of conjugated estrogens be changed to reflect two active estrogenic components, estrone sulfate and equilin sulfate, and no required concomitant components. The report also suggested that delta<sup>8,9</sup>-DHES and the over twenty other constituents of pregnant mares' urine be considered nothing more than impurities which in no way contribute to the drug's safety or efficacy.

45. Dr. Williams' report reached the same conclusion that FDA's internal Ad Hoc Committee, charged with the responsibility of examining the issue of approving a generic version of Premarin, reached earlier that week. FDA's committee concluded that the FDA should approve a generic version of Premarin. Similarly, an Advisory Committee to the FDA, convened to consider the importance of delta<sup>8,9</sup>-DHES and the ingredients that had to be present in a generic conjugated estrogens, in approximately 1996, concluded that there was no evidence presented to the FDA that supported that delta<sup>8,9</sup>-DHES had to be present in a generic conjugated estrogens.

46. In this way, Wyeth succeeded yet again in preventing a generic conjugated estrogens drug product from reaching the market. In so doing, Wyeth caused Duramed to waste tens of millions of dollars pursuing the ANDA, and precluded Duramed for years from selling a conjugated estrogens product on the market. To the present day, there is no generic alternative to Premarin — another example of Wyeth's monopoly of the U.S. conjugated estrogens market.

D. Wyeth Opposes New Drug Application and Prevents the Success of Duramed's Cenestin

47. In May 1997, Duramed decided to file a New Drug Application ("NDA") for a brand name conjugated estrogens drug that would be called Cenestin. Because of the ANDA's rejection, Duramed was forced to focus its attention on getting to market a name brand conjugated estrogens, albeit delayed by years, thereby further causing damages to Duramed. Importantly, the brand name drug market is slower in growth, and therefore market penetration is a more time-consuming and expensive endeavor.

48. From September 1997 to January 1998, Duramed performed extensive clinical tests to insure the efficacy of Cenestin for vasomotor symptoms. The brand name product Cenestin, like its generic predecessor, would be a plant-derived and less expensive drug treatment for menopausal

women. On or about March 30, 1998, Duramed submitted NDA No. 20-992 to FDA's Center for Drug Evaluation and Research. To obtain approval for an NDA, Duramed had to demonstrate the drug's safety and efficacy.

49. Wyeth would not relent in opposing Duramed's efforts to compete with its number one prescription drug Premarin. Within a few months of Duramed's filing of its NDA, Wyeth promptly filed another Citizen Petition with the FDA, this time challenging Duramed's application for the name brand drug Cenestin. In a desperate attempt to force the FDA to reject another of Duramed's applications, Wyeth requested that the FDA (a) require Duramed to conduct additional safety studies to support approval, (b) change the current USP definition of conjugated estrogens, and if the drug were approved, (c) preclude Duramed from using "conjugated estrogens" in the drug's name, and (d) require Duramed to label that Cenestin is not a substitute for Premarin.

50. On March 24, 1999, the FDA approved Duramed's NDA for Cenestin and rejected Wyeth's Citizen Petition. The FDA's decisions, however, did not deter Wyeth from hampering Cenestin's success on the market. The very next day following FDA's approval of Cenestin, on March 25, 1999, Wyeth issued a press release designed to discourage consumers from purchasing Cenestin. The press release, titled "Uniqueness of Premarin (conjugated estrogens tablets, USP) Confirmed" stated that even though the FDA had approved Cenestin, it was not the same as "Premarin, the most widely used estrogen replacement medication in the United States." The press release, touting the virtues of Premarin, such as its 56 years of clinical use and its 3,000 scientific studies, claimed that the "Duramed product, which bears the unbranded common (chemical) name 'synthetic conjugated estrogens, A,' is neither the branded equivalent to Premarin nor is it a generic equivalent."

51. Wyeth's efforts did not stop with this press release. As soon as Duramed obtained approval of its NDA for Cenestin, Wyeth's contracting strategy shifted to one that prevents health plans and PBMs from adding Cenestin to their formularies and making it available to their members as an alternative conjugated estrogens to Premarin.

52. To prevent sales of Cenestin and to maintain monopoly position, Wyeth has used its market power to enter into contracts with managed care organizations, employers, other entities offering health plans and PBMs to prevent them from making Cenestin available to their members and to limit the sales of Cenestin.

53. In the face of escalating prescription drug costs, health plans have turned to the formulary management process to control both drug product utilization and costs. The drug product formulary is a list of required, preferred or recommended drugs for health plan members. Inclusion on a drug product formulary typically involves a review to select the drug products that will produce the desired therapy at a reasonable cost.

54. PBMs administer the pharmacy benefits (and formularies) for health plans. PBMs contract with a given health plan to manage the pharmacy benefits program for that health plan's members. PBMs also put together networks of participating pharmacies. In exchange for being included in the network, the participating pharmacies agree to fill pharmaceutical prescriptions at a discount. PBMs also establish formularies. Because PBMs administer the pharmacy benefits for a substantial percentage of health plans and their members within the United States, to compete successfully, manufacturers need to have their pharmaceutical drug products listed on the formularies established by PBMs.

55. Today, over 70% of all Americans have their purchase of prescription drug products controlled through the use of a formulary program. Patients receiving prescription drug products not listed on their health plan's formulary are often subjected to higher out-of-pocket expenses. These higher costs function to encourage members to use the drug products on formulary. Whether a drug product is listed on a formulary also influences physicians' decisions as to which drug to prescribe.

56. The ability of a manufacturer to market effectively its drug products depends on securing favorable formulary and reimbursement status from the health plans in the market. This is especially true of new drug products, where early physician access is critical to the ultimate success of the product.

57. Recognizing the importance of Cenestin's placement on formularies, as soon as Duramed received FDA approval to market Cenestin, it began to promote aggressively its product. To assist in the promotion of its new drug, in approximately March 1999, Duramed retained the services of Cardinal Marketforce to acquaint physicians with Cenestin. In October 1999, Solvay Pharmaceuticals, Inc. began working with Cardinal to accomplish this task. Also in April 1999, Duramed retained the services of Viking Healthcare Solutions ("Viking") to aid the process of getting Cenestin on formularies of health plans and PBMs, to make calls on accounts (primarily wholesalers and retailers) to whom Duramed sells its drugs, to negotiate its managed care contracts, and otherwise to assist Duramed in successfully competing with Premarin. Cenestin's placement on formularies is critical to insure its success in the market, and would enable it to access approximately 125 million health plan members who could take advantage of the plant-derived, lower cost conjugated estrogens drug.

58. Wyeth currently holds contracts with most of the health plans and PBMs representing a substantial majority of the covered lives in the United States. These contracts cover most of the health plan members in the United States. Duramed has had little success acquiring such contracts because of Wyeth's anti-competitive and exclusionary conduct. Wyeth has entered into contracts with health plans and PBMs that provide that Premarin shall be the sole and exclusive conjugated estrogens on formulary. These exclusive contracts target the exclusion of Cenestin from the market. As Cenestin is the only competing conjugated estrogens, Wyeth's conduct has the purpose and effect of excluding only Cenestin. In this way, Wyeth assures that Premarin rather than Cenestin will be dispensed to consumers.

59. In order to obtain exclusive contracts, Wyeth has offered rebates, discounts, fees and other benefits to health plans and PBMs upon the condition that Premarin be the sole and exclusive conjugated estrogens on their formularies. These rebates, discounts and fees are computed based on the dollar or unit volume of sales of Premarin to plan members. Because Premarin holds a large market share and has a substantial volume of sales, denial of these rebates, discounts or fees to the health plans or PBMs would result in an enormous financial loss. Thereby, Wyeth has imposed an enormous hurdle on health plans and PBMs that desire to add Cenestin to their formularies and has effectively foreclosed Cenestin from being included on such formularies.

60. Further, Wyeth has employed "disguised" exclusive contracts by offering rebates, discounts, or fees only on the condition that health plans or PBMs enter into contracts requiring use of Premarin by the health plan's members in a percentage equal to Premarin's national market share, with additional incentives for exceeding that market share. These contracts subject health plans and PBMs to enormous financial penalties for permitting sales of Premarin to drop below the national

market share for Premarin, which would happen, if for instance, they permitted a competing drug product such as Cenestin on their formularies. In this way, Wyeth forces health plans and PBMs to promote sales of Premarin, and to ignore the only other conjugated estrogens tablet on the market—Cenestin.

61. In addition to the contractual language described above, Wyeth informs health plans and PBMs that they will lose moneys associated with rebates and administrative fees tied to sales of Premarin if they add Cenestin to their formularies, thereby discouraging the plans and PBMs from adding Cenestin. Despite lower wholesale prices, the non-inclusion on formularies makes Cenestin less affordable for consumers at the retail (pharmacy) level, discourages physicians from prescribing Cenestin, and thereby precludes consumers from purchasing Cenestin.

62. In addition to these exclusive and “disguised” exclusive contracts, Wyeth has also misrepresented the characteristics and therapeutic qualities of Premarin and Cenestin to enhance the sales of Premarin, to restrict the sale of Cenestin, and to maintain Wyeth’s monopoly power.

63. Following these efforts to hinder Cenestin’s success in the market, Wyeth has continued to benefit from its monopoly of the conjugated estrogens market and has increased the price for Premarin on three (3) separate occasions in the 1999-2000 time period alone. Between January 1999 and January 2000, Premarin experienced one of the largest price increases of any single source prescription drug—12.1 %, a rate which is 5 ½ times the rate of inflation. Effective March 29, 2000, Wyeth raised Premarin’s price by 6.2%.

64. Despite aggressive promotion of Cenestin, Duramed has been unable to achieve the anticipated and projected sales for its product because of Wyeth’s exclusive and “disguised” exclusive contracts. These contracts are the primary impediment to Cenestin’s access to these

managed care health plans. Accordingly, Wyeth's exclusive and "disguised" exclusive contracts preclude Cenestin's access to a majority of formularies that would enable it to compete effectively with Premarin in the market place. In the aforementioned ways, Wyeth's pervasive pattern of misconduct has allowed it to maintain its predominance in the market by monopolizing the conjugated estrogens market with its exclusionary and anti-competitive conduct that continues to the present day.

V.  
**CLAIMS FOR RELIEF**

Count I: Monopolization

65. Duramed realleges paragraphs 5-64. The relevant geographic market is the United States. Duramed and Wyeth compete on a nationwide basis in selling conjugated estrogens drug products. The market is properly limited to the United States since under the FDCA, manufacturers of pharmaceutical drug products are prohibited from selling and distributing their drug products in the United States without the FDA's approval.

66. The product market in this case is conjugated estrogens prescription drugs, of which Wyeth possesses approximately a 99% share. Conjugated estrogens are the only modified release estrogen replacement drug products. Modified release estrogen replacement drug products allow estrogen to remain in the female system on a continual basis until the next dose is taken (usually 24 hours) and, therefore, are effective in the treatment of vasomotor symptoms, such as hot flashes and night sweats. Because there are no interchangeable substitutes for conjugated estrogens medication in the treatment of vasomotor symptoms in menopausal women, the product market is properly limited to conjugated estrogens.

67. In the alternative, Duramed alleges that the relevant product market is the oral estrogen replacement therapy ("Oral ERT") market, of which Wyeth's Premarin has approximately an 82% market share. The Oral ERT market is comprised of those estrogen replacement drug products which are administered orally (in tablet form). These oral drug products are considered by many health care professionals to provide cardiovascular benefits that drug products administered through other methods, including the patch, do not provide. As a result, the estrogen replacement drug products which are not taken orally are not reasonably interchangeable with Oral ERT products.

68. Further, in the alternative, Duramed alleges that the relevant product market is comprised of all estrogen replacement products (ERT). The ERT market is made up of conjugated estrogens and other estrogen-based pharmaceutical drug products which are used primarily to treat vasomotor symptoms. The ERT market includes estrogen replacement drug products that are administered in oral, patch, vaginal ring and gel or cream form.

69. Finally, in the alternative, Duramed alleges that the relevant product market consists of conjugated estrogens, estrogen/progesterone combination drug products such as Prempro and Premphase and other estrogen-based pharmaceutical drug products which are used primarily to treat the vasomotor effects of menopause (hot flashes and night sweats).

70. Wyeth has monopoly power in each of the alleged markets.

71. By engaging in the unlawful anti-competitive and exclusionary conduct, in violation of the antitrust laws contained in 15 U.S.C. § 2, set forth in paragraphs 51-64 of this complaint, Wyeth has willfully maintained monopoly power. Wyeth is a monopolist because, as evidenced by the conduct described in paragraphs 51-64 of this complaint, it has effectively excluded competition

from the relevant market, thereby maintaining its dominant market share in the relevant market, and has profited by its anti-competitive conduct by raising Premarin's prices and reaping the benefits of its illegal monopoly. The barriers to entry in the relevant market have also prevented competition. These barriers to entry include, but are not limited to, the requirement of FDA approval for marketing prescription drugs, patents obtained by manufacturers of branded prescription drugs, and the necessity of manufacturers of prescription drugs securing placement on formularies of health plans and PBMs that constitute a majority of the third-party payors of prescription drug products, and other health care expenses.

72. Wyeth's conduct has proximately caused damages to Duramed in an amount to be proved at trial.

Count II: Attempted Monopolization

73. Duramed realleges paragraphs 5-72, and the relevant market allegations in paragraphs 65-70. As alleged in paragraphs 51-64 of this complaint, Wyeth has engaged in anti-competitive and exclusionary conduct with a specific intent to monopolize the relevant market (as defined above), and has created a dangerous probability of achieving a monopoly, in violation of the antitrust laws contained in 15 U.S.C. § 2.

74. Wyeth's conduct has proximately caused Duramed's damages in an amount to be proved at trial.

Count III: Violation of Sherman Act's § 1

75. Duramed realleges paragraphs 5-74. As alleged in paragraphs 51-64 of this complaint, Wyeth has entered into exclusive and "disguised" exclusive contracts with health plans

managed care and PBMs that have resulted in unreasonable restraints of trade and competition in interstate commerce in violation of the antitrust laws contained in 15 U.S.C. § 1.

76. Wyeth's conduct has proximately caused damage to Duramed in an amount to be proved at trial.

Count IV: Clayton Act § 3

77. Duramed realleges paragraphs 5-76. As alleged in paragraphs 51-64 of this complaint, Wyeth has made contracts for the sale of Premarin and has established prices, discounts, rebates, and fees on the condition that PBMs, health plans, and health plan members not use, deal in, or purchase Cenestin. The effect of such conduct has been to lessen competition substantially and to tend to create a monopoly in the relevant markets alleged above, in violation of Clayton Act § 3, contained in 15 U.S.C. § 14.

78. Wyeth's conduct has proximately caused damage to Duramed in an amount to be proved at trial.

**DEMAND FOR RELIEF**

Plaintiff Duramed respectfully requests that this Court find that Wyeth's conduct is in violation of the antitrust laws alleged in this complaint, award Duramed actual and treble damages proximately caused by Wyeth's conduct that is violative of the antitrust laws, permanently enjoin Wyeth from engaging in anti-competitive and exclusionary conduct as provided for in 15 U.S. C. § 26, and award Duramed costs of the suit, simple interest on actual damages, and reasonable attorneys' fees as provided for in 15 U. S. C. § 15, and such other and further relief to which Duramed may be justly entitled.

**DEMAND FOR JURY TRIAL**

Duramed requests a trial by jury on all triable issues alleged in this complaint.

Dated: September 5, 2000

Respectfully submitted,



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